

Translation

PATENT COOPERATION TREATY

PCT/JP2003/013416



PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NTK03-1564WO	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2003/013416	International filing date (day/month/year) 21 October 2003 (21.10.2003)	Priority date (day/month/year) 24 October 2002 (24.10.2002)
International Patent Classification (IPC) or national classification and IPC A61K 45/00, 38/17, A61P 35/00, 37/04		
Applicant EFFECTOR CELL INSTITUTE		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

a. ☐ (sent to the applicant and to the International Bureau) a total of \_\_\_\_\_ sheets, as follows:

☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b. ☒ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) Disc 1, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒ Box No. I Basis of the report

☐ Box No. II Priority

☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

☐ Box No. IV Lack of unity of invention

☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

☐ Box No. VI Certain documents cited

☐ Box No. VII Certain defects in the international application

☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 08 April 2004 (08.04.2004)	Date of completion of this report 20 December 2004 (20.12.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2003/013416

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ The international application as originally filed/furnished
- ☐ the description:
- pages \_\_\_\_\_, as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the claims:
- pages \_\_\_\_\_, as originally filed/furnished
- pages\* \_\_\_\_\_, as amended (together with any statement) under Article 19
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- pages \_\_\_\_\_, as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP03/13416

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)

Claims

1-19

YES

Claims

NO

Inventive step (IS)

Claims

5, 6, 11, 12, 17, 18

YES

Claims

1-4, 7-10, 13-16, 19

NO

Industrial applicability (IA)

Claims

1-19

YES

Claims

NO

## 2. Citations and explanations (Rule 70.7)

Document 1: "Selective Recruitment of Immature and Mature Dendritic Cells by Distinct Chemokines Expressed in Different Anatomic Sites," (Marie Caroline Dieu, et al.), J. Exp. Med., 1998, Vol. 188, No. 2, pages 373-386

Document 2: "Macrophage-tropic HIV Induces and Exploits Dendritic Cell Chemotaxis," (Chen Lung Line, et al.), J. Exp. Med., 2000, Vol. 192, No. 4, pages 587-593

Document 3: WO, 01-83548, A1 (Effector Cell Institute), 8 November, 2001 (08.11.01)

Document 4: "BB-10010: An Active Variant of Human Macrophage Inflammatory Protein-1 $\alpha$  with Improved Pharmaceutical Properties," (M. G. Hunter, et al.), Blood, 1995, Vol. 86, No. 12, pages 4400-4408

## Inventive Step

Claims 1-4, 7-10, 13-16 and 19

Document 1 describes that MIP-1 $\alpha$  enhances the chemotaxis of a dendritic cell precursor (page 373, Abstract, Figure 1).

Document 2 describes that RANTES enhances the chemotaxis of a dendritic cell precursor (Fig. 1).

Document 3 describes that if an amphipathic polymer such as a partially butyl-esterified styrene-maleic acid copolymer is used to modify a cell chemotactic factor such as IL-8 or MIP-1 $\alpha$ , the activity of the said factor is sustained (claims 1-15, page 4, line 18).

Document 4 describes that BB10010 that is a functional derivative of MIP-1 $\alpha$  is a derivative suitable for preparations improved, for example, in the solubility posing a problem with MIP-1 $\alpha$  (page 4400, Abstract).

In this regard, the applicant (1) states in the written reply dated 14 September, 2004 that even if, for example, MIP-1 $\alpha$  that is also a chemotactic factor for neutrophils is administered, the number of neutrophils in peripheral blood does not increase, and (2) insists that even if cell chemotactic action occurs *in vitro*, the action does not always occur *in vivo*.

However, before the filing date of the present application, in the field of drugs, it is a technique well known to a person skilled in the art that a dendritic cell precursor collected from peripheral blood is used for, for example, immunotherapy, and it is also considered to be an issue well known to a person skilled in the art to efficiently collect the said precursor when the said therapy is practiced. So, a person skilled in the art could have easily conceived of enhancing the chemotaxis of a dendritic cell precursor and administering any of various factors having an action to induce the said precursor or any of their derivatives into blood for increasing the concentration of the said precursor in blood.

Furthermore, since the specification of the present application supports only MIP-1 $\alpha$  and BB-10010 as the factors that increase the level of a dendritic cell precursor in blood actually also *in vivo*, it is not considered that the effect of the subject matters of claims 1-4, 7-10, 13-16 and 19 containing a factor other than the said MIP-1 $\alpha$  and BB-10010 as an active ingredient is a special effect that could not have been predicted by a person skilled in the art.

## Supplemental Box Relating to Sequence Listing

## Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing
    - ☐ contained in the international application as filed
    - ☒ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purpose of search and/or examination
    - ☐ received by this Authority as an amendment\* on \_\_\_\_\_
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

*\* If item 4 in Box No. 1 applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*